site modulates the expression of said prokaryotic RNA, wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA.

REMARKS

Claims 27-29, 35-41, and 43-67 are pending. Applicants ask that claim 27 be amended. The basis for the amendment can be found, for example, at page 2, lines 17-25.

Edited Figures 4 and 5A are submitted in marked-up form herewith. The figures have been amended to remove the alleged new matter and are believed to overcome the objections of record.

The present invention recognizes that there are RNA molecular interaction sites present in a selected organisms as well as at least one other organism which serve as a binding site for a molecule which, when bound to site, modulates the expression of the RNA. For reasons explained extensively in the specification, identification of these sites—having, as they do, inter-species commonality—gives rise to powerful tools for employment in therapeutics and diagnostics.

Claims 35-41 and 43-67 are rejected under 35 U.S.C. § 112, first paragraph. The Office Action alleges that the specification does not describe that the oligonucleotide's molecular interaction site can be other than the iron response element or the 3' untranslated region of histone RNA. Applicants traverse the rejection. The standard for determining compliance with the written description requirement of section 112 is whether a claim defines an invention that is clearly conveyed to those skilled in the art at the time the application was filed. See, *e.g., In re Gosteli*, 872 F.2d 1008, 1012, 10 U.S.P.Q.2d 1614, 1618 (Fed. Cir. 1989). Further, it is established law that limitations appearing in claims need not be literally recited in the specification. The issue is not whether words used in the claims are present in the specification but, rather, whether the ***concept*** expressed by the words is present. *In re Anderson*, 176 U.S.P.Q. 331 (C.C.P.A. 1973).

The specification states that the iron response element is an example of a typical RNA responsive element and that the iron response element is found in certain mRNAs associated with iron metabolism (e.g., page 32, lines 6-7 of the specification). It clearly follows that the inventors knew that other responsive elements other than the iron response element existed, and that not all RNA contained this element. Thus, the iron response element is an identified species of the genus of responsive elements. Instant claims 35-41 and 43-51 properly exclude the iron response element species from the scope of the claim. For at least this reason, applicants respectfully submit that the rejection should be withdrawn.

Claims 35-40, 43-57, and 59-67 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by, or alternatively, under 35 U.S.C. § 103(a) as allegedly obvious over Manzella et al., J. Biol. Chem., 1992, 267, 7077-7082 (the Manzella reference). Applicants respectfully request reconsideration because the Manzella reference does not teach or suggest applicants' claimed invention.

The Manzella reference, for example, does not teach or suggest a molecular interaction site that modulates the expression of RNA. As admitted by the Examiner in the Final Rejection, the Manzella reference does not disclose the modulation of the expression of ornithine decarbocylase mRNA by binding of a protein (page 6 of the January 15, 2003 Final Rejection). While Manzella et al. expressed the possibility that a cellular protein could bind to ODC mRNA 5'-UTR and regulate its translation in some way (page 7077, second column), they did not conclude that the binding of the protein produced a regulatory effect. Indeed, the Manzella reference states that they were unable to "ascribe a function to the protein."[1] (page 7081, second column). Thus, the Manzella reference actually teaches away from applicants' invention.

Despite the lack of disclosure, the Office Action alleges that the modulation function is inherent in the Manzella disclosure. As is well known, when the Office seeks to fill a gap in a disclosure with alleged intrinsic evidence, such evidence must make clear that the missing

[1] Further, applicants note that the Manzella reference speculated that the binding might result in a "sulfhydryl switch" like the iron responsive element (page 7081, second column), an element specifically excluded from claim 35. Thus, even if the binding molecule did have an impact, Manzella does not ascribe any claimed function to it.

descriptive matter is necessarily--always--present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill in the art. In re Oelrich, 40 U.S.P.Q. 323 (C.C.P.A. 1981); Continental Can Co. USA Inc. v. Monsanto Co., 20 U.S.P.Q.2d 1746 (Fed. Cir. 1991). The Office Action did not establish this. Significantly, the Manzella reference teaches that the regulatory function of their studied molecule is unknown. Further, applicants note the low expression (10-15% of wild binding activity) was found in the Manzella reference's use of 30 base sequences having the conserved heptmer of 69RNA (page 7081, column 1). It does not follow that one of ordinary skill would understand that the modulation function is ever present in Manzella's system much less always so. Because the Manzella reference does not disclose the instant claims directly or inherently, Applicants submit that the rejection should be withdrawn.

Claims 27-29, 35-38, 41, 43-55, and 58-67 stand rejected under 35 U.S.C. § 102(b) as allegedly anticipated by Garcia et al., J. Mol. Biol., 1995, 254, 247-259 (the Garcia reference), or alternatively, under 35 U.S.C. § 103(a) as allegedly obvious over the Garcia reference in light of Molecular Cell Biology and Textbook of Biochemistry. Even though applicants do not agree with the rejection, applicants ask that claim 27 be amended to add the following language "wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA." Because the Garcia reference is directed to initiation of translation (page 247, abstract), applicants believe that this amendment even more clearly distinguishes the instant claims from the cited art. As such, applicants respectfully request reconsideration and withdrawal of the rejection as it applies to claims 27-29.

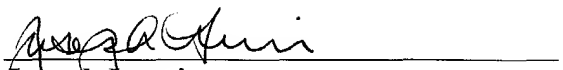
As discussed in the previous paragraph, the Garcia reference concerns RNA translation. One skilled in the art knows that translation concerns production of RNA molecules. In contrast, the instant claims are directed to binding interactions that modulate the expression of RNA. Modulation of expression in this context concerns altering the production of RNA products, not RNA itself. Thus, the Garcia disclosure is outside the scope of the instant claims. Nothing in presented from Molecular Cell Biology or Textbook of Biochemistry that cures this defect. For

at least this reason, applicants request reconsideration and withdrawal of the rejections as they apply to all claims.

Attached hereto is a marked-up version of the changes made to the specification and claims by the current amendment. The attached page is captioned **"VERSION WITH MARKINGS TO SHOW CHANGES MADE."**

Applicants respectfully submit that the claims are in condition for allowance. An early notice of the same is earnestly solicited.

Respectfully submitted,



Joseph Lucci
Registration No. 33,307

John W. Caldwell
Registration No. 28,937

Date: **March 17, 2003**

WOODCOCK WASHBURN LLP
One Liberty Place - 46th Floor
Philadelphia, PA 19103
Telephone: (215) 568-3100
Facsimile: (215) 568-3439

VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Figures

Please amend Figures 4 and 5A as presented in the attached pages.

In the Claims

Please amend claim 27 as follows.

27. An oligonucleotide comprising a molecular interaction site that is present in prokaryotic RNA and in at least one additional prokaryotic RNA, wherein said molecular interaction site serves as a binding site for at least one molecule that when bound to said molecular interaction site modulates the expression of said prokaryotic RNA, wherein the binding of said molecule to said molecular interaction site does not modulate translation of said RNA.